therapy) was instituted and within two weeks the patient's alcohol-related pain had completely resolved.

Comment

The association between alcohol-related pain and Hodgkin's disease was first noted in 1950.[2] Published surveys that followed reported an incidence ranging from 15 percent to 30 percent.[3,4] More recent observations, however, suggest a much lower frequency in the range of 1.5 percent to 5 percent.[1,5] The decreasing incidence of this symptom has been ascribed either to a possible change in the natural history of the disease or to the fact that patients with Hodgkin's disease tend to be identified earlier.[1,6]

The pain induced by alcohol has been described as either sharp and stabbing or dull and aching. A patient frequently links the discomfort with alcohol ingestion and may voluntarily discontinue its use. Characteristically, the pain begins within minutes after a patient swallows some of an alcoholic drink and subsides within 30 minutes to a few hours. In our patient, the pain subsided despite his continuing to drink.

Retrosternal pain has been noted with mediastinal lymph node involvement whereas with diseased axillary or cervical nodes, pain may be felt in the shoulder, neck or arm. The abdomen and groin are also sites of alcohol-related pain, and back pain with or without radiation down the leg has been described. When disease is present at several sites pain may not be felt in all of them. An important observation is that tumor can invariably be identified at or near the site of the alcohol-related pain, if not at the time of initial presentation, then when relapse occurs.[5]

Several features seem to characterize patients with Hodgkin's disease who have alcohol-related pain. Nodular sclerosing Hodgkin's disease is the predominant histologic type, and a higher than expected incidence of mediastinal involvement has been reported.[3,5] More women than men tend to have this symptom despite a two-to-one male predominance for the disease.[5]

The pathogenesis of alcohol-related pain is not well understood, though it is believed to result from localized swelling with stretching of the capsule of the affected lymph nodes or increased pressure in diseased marrow that expands and produces bone pain. Visible swelling of involved lymph nodes has been observed after ingestion of alcohol in patients with alcohol-related pain and, in at least one instance, thermography recorded a rise in lymph node temperature.

Although alcohol-related pain is uncommon, this report is a reminder that this symptom may precede any other recognizable feature of Hodgkin's disease and consequently may be helpful in the early diagnosis of this potentially curable disease.

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Secondary Syphilis With Pulmonary Involvement

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REPORTS OF CASES of primary and secondary syphilis have been increasing in number in the United States for the past several years,[1] and because of this physicians are rediscovering the protean manifestations of this disease. Pulmonary involvement in acquired secondary syphilis is uncommon.[2] We report the case of a 39-year-old man who had secondary syphilis and bilateral infiltrates on a chest roentgenogram. Following penicillin therapy for syphilis, the pulmonary abnormalities cleared over several months. Clinical criteria for the diagnosis of acquired secondary syphilis of the lung are suggested.

Report of a Case

A 39-year-old homosexual man was seen in August 1980 because of malaise for the past six months and a 5.9-kg (13-lb) weight loss in the previous month. He noted no fever or chills but had frequent night sweats. Four months previously, numerous nonpruritic skin lesions had developed in the groin and spread in a migratory fashion to the abdomen, chest, back, arms, legs and scalp. He smoked two packs of cigarettes per day. He said he did not abuse drugs intravenously or otherwise. He lived with 24 cats in San Francisco and had traveled recently to the Midwest. He had had multiple anonymous sexual contacts during the preceding months. He was currently unemployed but had worked in a grocery store. On review of systems there was a chronic nonproductive cough of two to three years' duration.

It was learned from the Public Health Department that the patient had been treated previously for syphilis. In 1972 his VDRL titer was positive at a 1:4 dilution and he received intramuscularly two injections of 2.4 million units of benzathine penicillin G at an interval of a week. Subsequent serologic testing, shown in Table 1, showed a VDRL titer in 1978 that was positive at a 1:2 dilution with a strongly positive result on fluorescent treponemal antibody-absorption test. In October 1979 his VDRL was positive in a titer of 1:1,024 and he was treated as in 1972. A VDRL titer in June 1980 was 1:128. In early August 1980 it rose to 1:256 and several weeks later it had risen to 1:512.

On physical examination he appeared well developed, was in no acute distress and had normal vital signs. Multiple salmon-colored, indurated, annular 0.5- to

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2-cm macules were scattered over the chest, back, arms and legs. There was no hypoesthesia. The palms and soles were hyperkeratotic without distinct lesions. Marked nontender mobile axillary, inguinal, epitrochlear and femoral lymphadenopathy was present. The lungs were clear. Similar maculopapular lesions without ulceration were seen on the shaft of the penis and on the scrotum. There was no penile discharge. No other abnormalities were detected.

TABLE 1.—*VDRL Titers of a 39-year-old Man With Syphilis With Pulmonary Involvement (San Francisco Public Health Department Records)*

Date	VDRL Titer	Date	VDRL Titer
1972	1.4*	Aug 27, 1980	1:512*
1978	1:2	Dec 1980	1:32
Oct 1979	1:1,024*	Mar 1981	1:16
Jun 1980	1:128	Aug 1981	1:16
Aug 1, 1980	1:256		

*Patient received penicillin therapy.

Laboratory evaluation gave the following results: erythrocyte sedimentation rate, 52 mm per hour; VDRL, 1:512; hemoglobin level, 13.6 grams per dl, and leukocyte count 9,900 per μl with a normal differential count. Chest roentgenograms showed a definite lingular infiltrate and a probable right lower lobe infiltrate (Figure 1, top).

The patient was admitted to hospital for further evaluation. Results of chemistry (SMA-6 and SMA-12) analyses, thyroid function tests and urine analysis were within normal limits. The electrocardiogram showed no abnormalities. Purified protein derivative (5 tuberculin units) and coccidioidomycosis skin tests were negative; *Candida* skin test was positive. Complement-fixation titers were negative for coccidioidomycosis and histo-

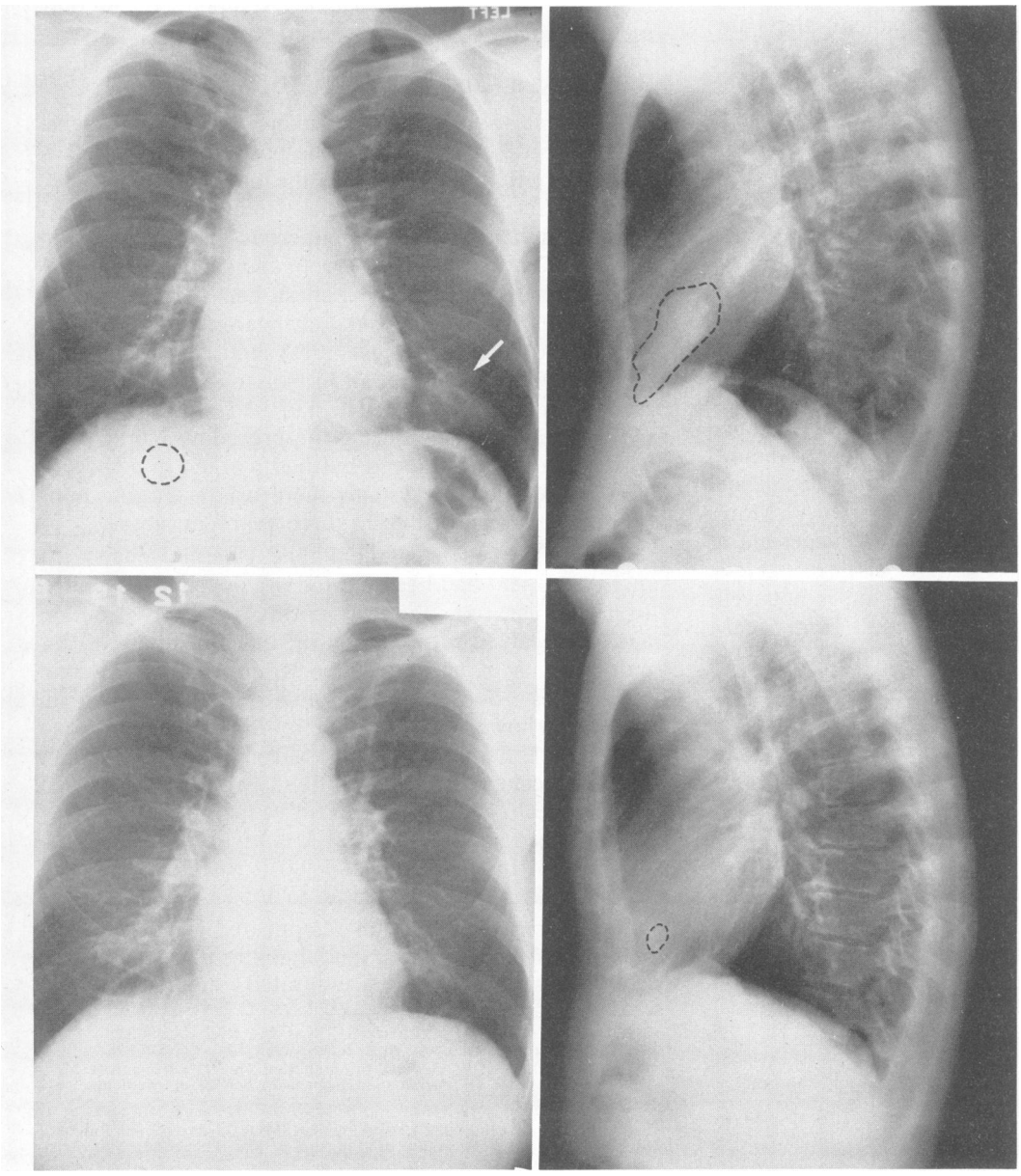

Figure 1.—Top, Chest roentgenogram showing definite lingular infiltrate **(arrow)** and probable right lower lobe infiltrate **(dotted circle). Bottom,** Chest roentgenogram four months later showing resolution of right lower lobe infiltrate and nearly complete resolution of the lingular process **(dotted circle).**

plasmin; heterophil and hepatitis B surface antigen test results were negative; and *Toxoplasma* fluorescent antibody IgG test was positive (titer 1:64). Pulmonary function testing showed no abnormalities. The patient produced no sputum for analysis. Analysis of a cerebrospinal fluid specimen, obtained to exclude asymptomatic central nervous system involvement, showed no cells, normal glucose and protein levels and negative results on cytology examination, VDRL test and culture. A biopsy specimen of involved skin showed a round cell infiltrate with a prominent plasma cell component in the papillary dermis, typical of secondary syphilis.

Because of the patient's multiple sexual contacts, we interpreted the fourfold rise in VDRL titer after the previous decline as evidence of luetic reinfection. Benzathine penicillin G, 2.4 million units, was injected intramuscularly and within six hours the patient became febrile to 38.2°C and his skin rash became more erythematous. Within 24 hours the patient's temperature returned to normal and his rash began to fade. Further investigation of the pulmonary infiltrates was deferred pending evaluation of the response to penicillin therapy. His hospital course was otherwise uncomplicated.

Following discharge, the patient's malaise and night sweats resolved and he regained 3.6 kg of weight. The rash cleared by December 1980. A chronic nonproductive cough and minimal lymphadenopathy have persisted. The sedimentation rate returned to normal and the VDRL titer fell to 1:32 by December. Serial chest roentgenograms done in October and December 1980 showed gradual resolution of the pulmonary infiltrates (Figure 1, bottom). The patient refused to return for further evaluation. Subsequent serologic testing by city health authorities recorded a further decline in VDRL titer to 1:16 by March 1981 and persistence of the VDRL titer at that level in August 1981.

Discussion

The first historical description of syphilis is a matter of debate. According to Cleugh,[3] no definite evidence had been found for this disease before 1495, and Smith[4] thought that it was first known around the time of the Reformation (16th century). Initially called by multiple names such as the "French disease," "Italian disease" or "Spanish disease,"[4] its current name is derived from the 1530 poem by Girolamo Fracastoro, *Syphilis sive Morbus Gallicus,* in which the shepherd Syphilus is afflicted with the disease.[3]

Porter[5] in 1885 was one of the first Americans to discuss acquired pulmonary syphilis. Subsequent studies evaluating necropsy specimens from the general population have estimated the prevalence of syphilitic lung disease at 0.55 percent.[6-9] The prevalence in autopsy studies on persons known to have had syphilis varies from 1 percent to 12.5 percent.[6-9]

Discussions of pulmonary syphilis are usually directed to tertiary disease stages. In 1920 Karshner and Karshner[10] remarked that secondary pulmonary syphilis can be "dismissed with a word. In a few of the cases mild bronchitic symptoms date from the period of exanthem." Earlier, Dieulafoy[11] reminded physicians that pleurisy may occur during the secondary stages and that bronchitis may be one of the earliest manifestations of syphilis, but parenchymal disease only appears in the advanced tertiary stages. Claytor[12] reported that the usual time from onset of disease to pulmonary involvement is 5 to 10 years, with cases occasionally noted as early as 1 or as late as 20 years after the appearance of a chancre. Karshner and Karshner[10] described four cases of pulmonary involvement within a year of onset of disease, however, and Olsan and Chambers[8] noted seven cases of early lues with pulmonary involvement. More recently, Biro and co-workers[2] discussed the case of a patient who had secondary syphilis and pulmonary involvement.

Diagnostic criteria for secondary syphilis of the lung are not available. Howard,[6] studying patients who had predominantly tertiary disease, suggested that a diagnosis of pulmonary syphilis should be considered when the following are present: clinical pulmonary involvement occurring without fever, sweats or emaciation; sputum negative for tubercle bacilli; other stigmata and serologic evidence of syphilis. A therapeutic trial is then undertaken. Morgan and colleagues[13] more recently noted that if a patient

> has a suggestive clinical picture, positive serological tests, and a persistently negative sputum for tubercle bacilli, if the radiological lesion clears decisively under antisyphilitic treatment, there are reasonable grounds for diagnosing pulmonary syphilis.

Similar criteria for the diagnosis of pulmonary syphilis, based largely on experience with tertiary disease, have been proposed by Hartung and Freedman[7] and Pearson and DeNavasquez.[14]

Based on the above criteria, we propose that the following be used as guidelines for the clinical diagnosis of secondary luetic involvement of the lung: (1) historical and physical findings typical of secondary syphilis, (2) serologic tests positive for syphilis, (3) pulmonary abnormalities seen radiographically with or without associated pulmonary symptoms or signs, (4) exclusion of other forms of pulmonary disease when possible by findings of serologic tests, sputum smears and cultures, and sputum cytology examination and (5) therapeutic response of radiologic findings to antisyphilitic therapy.

The diagnosis of syphilis in our patient was based on a fourfold rise in VDRL titer, skin lesions clinically and pathologically typical of secondary lues, development of a mild Jarisch-Herxheimer reaction with treatment and a subsequent fall in VDRL titer. Further evaluation elicited no other cause for the pulmonary infiltrates that resolved within several months of the penicillin therapy. This time course is similar to that described by Biro and associates.[2]

Considering the recent increasing incidence and recognition of primary and secondary syphilis (33.4 percent more cases diagnosed in 1980 than in 1977), especially among homosexual men,[15] it is likely that luetic pulmonary involvement will also appear with increasing frequency. Given the potential for diagnostic

confusion with entities such as lymphoma, sarcoid or, among homosexual men, cytomegalovirus infection or *Pneumocystis carinii* pneumonia, the clinical diagnostic criteria we suggest may prove useful.[16]

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Acute Renal Failure Following Repeated Streptokinase Therapy for Pulmonary Embolism

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PREVIOUS REVIEWS[1,2] have described the benefits and risks of administering fibrinolytic agents to bring about clot dissolution in both arterial and venous disease. As activators of the conversion of plasminogen to plasmin, these agents produce major side effects that include varying degrees of hemorrhage. Other complications, particularly with the use of streptokinase, are pyrogenic and allergic reactions, including anaphylaxis.[3] In this report we describe the case of a patient in whom a pyrogenic reaction and acute renal failure developed after he received streptokinase on the second of two occasions for pulmonary embolism.

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Report of a Case

A 38-year-old man was admitted to our hospital because of the recent onset of chest pain. Further history disclosed a contusion of the right calf that was followed by several episodes of localized pain and swelling. On the day of admission, his chest pain and associated symptoms were typical of angina pectoris. On examination in the coronary care unit, the respiratory rate was 40 per minute, the pulse was 88 per minute and the blood pressure was 100/88 mm of mercury. There was no jugular venous distention. The lungs were clear to auscultation. The point of maximal cardiac impulse was not displaced, the first and second heart sounds were normal and a fourth heart sound was present at the apex. No murmurs or friction rubs were audible. Peripheral pulses were normal. The lower extremities were not tender and there was no evidence of edema, erythema or localized calor. The remainder of the examination findings were unremarkable.

An electrocardiogram showed normal sinus rhythm, pronounced left axis deviation, deeply inverted T waves in leads V_1 through V_4, and deep S waves in leads V_5 and V_6. A portable chest x-ray study showed no abnormalities. The hemogram, sedimentation rate, serum urea nitrogen, serum creatinine and analysis of urine gave normal values. An arterial blood gas determination made while the patient was breathing room air showed that the partial pressure of oxygen (Pao_2) was 71 mm of mercury, the partial pressure of carbon dioxide ($Paco_2$) was 28 mm of mercury and the pH was 7.47. Creatine kinase was 107 IU per liter (normal, 225 or less), lactic dehydrogenase was 248 IU per liter (normal, 200 or less) and aspartate aminotransferase (formerly, SGOT) was 28 IU per liter (normal, 41 or less). Serial cardiac enzyme determinations did not suggest an acute myocardial infarction.

During the first two hospital days, angina-like chest pain continued to recur but was relieved by the sublingual use of nitroglycerin. On the third hospital day a cardiac catheterization was done. All right heart pressures were moderately elevated. The pulmonary artery pressure was 59/27 mm of mercury, with a mean pressure of 34 mm of mercury. Pulmonary angiography showed large embolic filling defects in the right and left proximal pulmonary arteries with smaller filling defects in the branch vessels supplying the right and left upper lobes and the left lower lobe. Findings on left ventriculography and coronary arteriography were normal. Streptokinase therapy was begun, with a loading dose of 250,000 units and an hourly infusion of 100,000 units. After two hours there was bleeding from the femoral arterial and venous catheterization sites that could not be controlled. Administration of the drug was discontinued, and continuous infusion of heparin was begun to maintain the partial thromboplastin time in the range of 1½ to 2½ times the control values.

On the 11th hospital day, pain in the patient's right calf, acute chest pain and dyspnea recurred. There was a palpable tender cord in the right popliteal area. An